(19) World Intellectual Property Organization International Bureau





(43) International Publication Date 18 December 2003 (18.12.2003)

PCT

(10) International Publication Number WO 03/104432 A2

(51) International Patent Classification7:

(21) International Application Number: PCT/US03/18373

(22) International Filing Date: 9 June 2003 (09.06.2003)

(25) Filing Language:

í

English

C12N

(26) Publication Language:

English

(30) Priority Data:

60/387,293 60/411,032 7 June 2002 (07.06.2002) US 16 September 2002 (16.09.2002) US

(71) Applicant (for all designated States except US): THE GOVERNMENT OF THE UNITED STATES, AS REPRESENTED BY THE SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES [US/US]; Office of Technology Transfer, 6011 Executive Boulevard, Suite 325, Rockville, MD 20852-3084 (US).

(72) Inventors; and

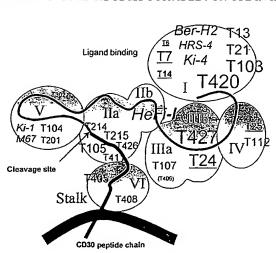
(75) Inventors/Applicants (for US only): PASTAN, Ira, H. [US/US]; 11710 Beall Mountain Road, Potomac, MD 20854 (US). NAGATA, Satoshi [JP/US]; 6070 California

Circle 413, Rockville, MD 20852 (US). ONDA, Masanori [JP/US]; 320 Lorraine Drive, Rockville, MD 20852 (US). NUMATA, Yoshito [JP/JP]; 2-451-1-311 Hirano Kashiwara, Osaka, Osaka 581-0019 (JP). SANTORA, Kenneth [US/US]; 10543 Wheatley Street, Kensington, MD 20895 (US). BEERS, Richard [US/US]; 5306 Russett Road, Rockville, MD 20853 (US). KREITMAN, Robert [US/US]; 11915 Reynolds Avenue, Potomac, MD 20854 (US). SINHA, Abhishek [US/US]; 11533 Aliento Court, San Diego, CA 92127 (US).

- (74) Agents: HYMAN, Laurence, J. et al.; Townsend and Townsend and Crew LLP, Two Embarcadero Center, 8th Floor, San Francisco, CA 94111 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),

[Continued on next page]

(54) Title: ANTI-CD30 STALK AND ANTI-CD30 ANTIBODIES SUITABLE FOR USE IN IMMUNOTOXINS



Location of topographical epitopes on CD30 molecule

(57) Abstract: CD30 is a receptor expressed on cells of Hodgkin's disease and certain leukemias. The extracellular portion of CD30 is cleaved, releasing a form known as sCD30. The invention relates in part to the discovery that a residual, extracellular "stalk" of CD30 remains after cleavage of sCD30. The stalk provides an advantageous and previously unrecognized target for immunotoxins. The invention provides antibodies that bind to the CD30 stalk or to epitopes destroyed upon the cleavage of CD30 which results in the stalk. The invention further provides new anti-CD30 antibodies that form effective immunotoxins and are particularly suitable for making disulfide stabilized Fv ("dsFv")-immunoconjugates. The dsFv immunoconjugates can be used as reagents to label CD30-expressing cancer cells or to inhibit the growth of CD30-expressing cancer cells. Moreover, the invention provides anti-CD30 antibodies that activate complement-dependent cytotoxicity.

Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE. AG. AL, AM, AT. AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH. CN. CO, CR, CU. CZ. DE. DK, DM, DZ. EC. EE, ES. FI. GB, GD, GE, GH, GM, HR. HU, ID. IL. IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS. LT, LU. LV, MA, MD, MG, MK, MN. MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU. SC, SD, SE, SG, SK, SL, TJ. TM, TN. TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW). Eurasian

patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations
- of inventorship (Rule 4.17(iv)) for US only

Published:

without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.